**REMARKS**

Claims 1-16 and 18-29 remain pending in the subject application, of which claims 1-9, 12-13, 15-16, 19-21 and 25-26 have been amended to more clearly recite what the applicant regards as his invention. Claim 17, which had duplicated the subject matter of claim 16, has been canceled. No new matter is added.

Applicants have considered all of the objections and rejections raised in the Office Action of June 8, 2007, and respond fully below.

Rejections under 35 U.S.C. § 112, First Paragraph

Claims 1-29 stand rejected under 35 U.S.C. § 112, first paragraph, for allegedly failing to comply with the enablement requirement. Applicants respectfully traverse.

At the outset, Applicants respectfully submit it is well-established that, for purposes of enablement, a specification need not teach or disclose what is well-known in the art or is within the knowledge of one of ordinary skill in the relevant art. See, for example, *Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 231 USPQ 81 (Fed. Cir. 1986), *cert. denied*, 480 U.S. 947 (1987). With this in mind, Applicants respond to the individual points raised in the Office Action, as follows.

First, the Examiner alleges that the specification does not teach what a "positive designator" is. However, Applicants respectfully point out that the specification discloses:

> The designators may be attached to the sample in any manner, may be physically attached, electronically attached, and attached in multiple ways. Physical attachment can be accomplished, for example, *by placing a marking on the sample vessel, or by attaching a label reflecting the designation to the sample vessel*. An apparatus may incorporate *a printing, engraving, etching or other apparatus for marking the vessel directly, and may incorporate a label printer or label attachment device for attaching a label to the vessel*. The designator may be *electronically attached to the vessel*, for example in an electronic memory, which may be attached to the vessel by correlation to a sample number, a sample position, or a code or other designation on the sample vessel. (Emphasis provided.)

Specification at page 13, line 24 to page 14, line 2.

Thus, the specification provides several examples of positive designators, such as labels or etchings or markings on the sample vessel, and also describes ways that the sample vessel may be labeled or etched or engraved. The specification does not need to specifically teach how

to engrave or etch a sample vessel or how to print a label, since those of ordinary skill in the art know how to label the sample vessel according to any of these disclosed techniques.

Next, the Examiner alleges that the specification does not teach how one having ordinary skill in the art would determine if the criteria for receiving a positive designator are met. Applicants respectfully submit that the specification teaches a system for carrying out the claimed method, where the system comprises, *inter alia*, an excitation source a detector array, and a means for comparing a result from the sample with the criterion. Specification at page 14, lines 14-19. The specification also discloses that:

> The criterion may be an absorbance, a transmittance, a reflectance, a degree of scattering, a luminescence, a fluorescence, an emission, or backscattering, and may be at a particular wavelength or selection of wavelengths.

Specification at page 11, line 29 to page 12, line 1. According to the specification:

> The means for comparing the result can comprise an electronic device, which may be a computer, that can receive a signal from the detector array and compare it to a criterion, which may be a value stored in a memory, which can be a fixed memory or a dynamic memory and can be provided by hardware or software, or the value may be obtained by comparison to a signal obtained from a control sample.

Specification at page 14, lines 14-19.

Applicants respectfully submit that it is well-known to those of skill in the art to shine a light from an excitation source through a sample, detect it with a detector, and obtain a result, and that more details are not necessary to enable one of ordinary skill in the art to practice the claimed invention. The specification teaches that once a detector obtains the result of the interrogation, a computer compares that result with a criterion, which may be a number stored in its memory. This comparison determines whether the criterion is met or not. It is also well within the skill of the ordinary artisan to use a computer for comparing a result with a stored number and determine whether the result is greater than or less than the stored number.

Finally, the Examiner makes an objection with respect to acetic acid and reducing agent. However, the last sentence of the first paragraph of page 2 of the Office Action is not complete, and Applicants *assume* that the Examiner intended to reject claims 10 and 11 on the basis that the specification does not allegedly teach what method is performed to determine if acetic acid or reducing agent are to be added. Applicants respectfully submit that those of ordinary skill in the art know the sample conditions that would require the addition of acetic acid or reducing

agent. Whereas heretofore the user had to manually determine whether the conditions for the addition acetic acid or reducing agent are met, the presently claimed invention provides for an *automated* method of determining the sample condition using spectrographic methods.

For the reasons set forth above, Applicants respectfully submit that the specification as originally filed enables the full scope of the pending claims, and respectfully request reconsideration and withdrawal of the rejections under 35 U.S.C. § 112, first paragraph.

Rejections under 35 U.S.C. § 112, Second Paragraph

Claims 1-29 stand rejected under 35 U.S.C. § 112, second paragraph, for allegedly being indefinite and, in particular, because the claims allegedly "do not describe what method steps are required to determine a positive indicator." Applicants respectfully submits that these rejections are overcome in part in view of the amendments to the claims, and respectfully traverses the remaining rejections.

Claim 1 has been amended to now more clearly recite "determining whether a result of said interrogation ~~to~~ meets a criterion" and "attaching a positive designator to the sample vessel if the result meets the criterion[.]" the remaining claims 2-16 and 18-29 depend (directly or indirectly) from claim 1.

Claims 2, 3 and 7 have been amended to remove the word "intended."

The dependence of claim 3 is corrected to provide antecedent basis for the word "assay." Beyond that, Applicants respectfully point out that the claimed method classifies a cytological sample as being suitable or unsuitable in its present condition for performing an assay, but performance of the assay itself is not part of the claimed method. For example, in accordance with claim 4, the cytological sample meets the criterion for performing an assay by having sufficient cells within it, e.g., so that a slide can be prepared to view the cells.

Applicants respectfully submit that claim 4, as amended, is clear and definite in view of the teachings of the specification, where it states:

> The positive designator may indicate that sufficient cells are present in the sample to permit performance of additional methods on the sample beyond an intended method for which the sample was designated; for example, the positive example may indicate that withdrawal of an aliquot of the sample for molecular testing may be performed prior subjecting the sample to automated slide preparation.

Specification at page 12, line 29 to page 13, line 4.

The claimed methods, therefore, determine whether sufficient cells are in the sample to conduct various tests on the sample.

Claim 5 has been amended to specify the cell types.

Claims 6 and 7 have been amended to clarify that the respective positive designator "indicates" that the sample is "satisfactory for ...." (claim 6) or adequate in quantity to allow for ...." (claim 7), and thus are now definite. Similar amendments have been made to claims 8 and 9 regarding the manipulation designators.

Further, with respect to claim 6, Applicants respectfully point out that the claims are not directed to measuring the positive designators. Instead, the sample vessel is marked with a respective positive designator or manipulation designator depending on the results obtained from interrogation of the sample. Once it is determined that the sample has met (or not met) the criterion, the samples are marked with the respective designator. Heretofore, this determination was made manually by lab technicians, which as the specification discloses, was time-consuming, error-prone, and inconvenient for the patient. What happens after the determination is made is not part of the claimed invention. What is part of the claimed invention is the automated method of classifying and marking sample vessel. Thus, the claims are not directed to a type of method used to determine adequate withdrawal of the sample (claim 7), method used to determine adequate withdrawal of the sample acquiring additional sample (claim 8), or a method performed to determined if treatment is required (claim 9). Instead, the claims are directed to determining in an automated fashion whether a sample meets a predetermined criterion for undergoing these processes.

Claims 12-13 and 15-16 have been amended to directly specify the criterion (i.e., "the criterion is ...." replaces "the criterion indicates ...."). The specification at page 11, line 27 to page 12, line 24 teaches how the respective criterions can be used and how the sample interrogation result can be compared with the criterion. By way of example, those of ordinary skill in the art know how to prepare line plots of spectrophotometric values, e.g., absorbance, transmittance, etc., versus a particular feature of a solution, e.g., the concentration of cells, mucus, blood, etc., and then set an acceptable threshold value for their particular application.

The Office Action states, "Claim 18 does not describe what the sample is mixed with." In response, Applicants respectfully point out that what is being claimed is that the sample itself is being mixed, i.e., so that any settled biological material, e.g., cells, blood, mucus, etc., are substantially uniformly distributed throughout the sample and are not settled at the bottom.

With respect to claim 22, Applicants respectfully submit that the specification explicitly teaches that the "attaching" of a positive or manipulation designator to the sample vessel may be electronic, instead of physical. For example, the specification states, "The designators may be attached to the sample in any manner, may be physically attached, electronically attached, and attached in multiple ways. *** The designator may be electronically attached to the vessel, for example in an electronic memory, which may be *attached* to the vessel by correlation to a sample number, a sample position, or a code or other designation on the sample vessel." (Specification page 13, line 24 to page 14, line 2) (Emphasis added).

Claim 25 has been amended to delete the offending "temporal conjunction" language.

In view of the foregoing amendments and remarks, Applicants respectfully request reconsideration and withdrawal of the rejections under 35 U.S.C. § 112, second paragraph.

Rejections under 35 U.S.C. § 102(b)

References Cited in the Specification

Claims 1-29 stand rejected under 35 U.S.C. § 102(b) for allegedly being anticipated by the references cited on page 15, lines 1-12, of the specification. Applicants respectfully traverse.

The Examiner cites the first part of the first sentence of the first paragraph on page 15 and the last sentence of the same paragraph for creating an anticipation rejection. Applicants respectfully submit that once the paragraph is read in its entirety, it would become clear that it does not anticipate the present claims. The paragraph in question states:

> An apparatus performing a method of the invention can be independent or can be integrated with additional components capable of performing further methods upon the sample. For example, the sample(s) can be further processed after its designation by an automated sample processor, and may be imaged by an automated imaging system. The automated classification system may be adapted to transfer the sample to an automated sample processor and/or imager, and can optionally be incorporated into such a system. Exemplary automated systems include Cytyc Corporation's ThinPrep® Imaging System, the TriPath FocalPoin™ Profiler, the ChromaVision Acis® System, the CompuCyt iCyte Imaging System, the Applied Imaging CytoVision™ System, and the Veracel Verasys Imaging System. The methods can be incorporated into sample processing devices such as those described in U.S. Pats. Nos. 5,185,084, 5,266,495, 6,010,909, 6,225,125, and 5,942,700, all assigned to Cytyc Corp.

First, the paragraph in question states that any apparatus used to perform the methods of the invention can be integrated with other components. These "other" components can include

an automated system that was used in the market as of the filing of the application, as exemplified in the above-quoted passage from the specification. The quoted passage does *not* say that an apparatus that can perform the (claimed) methods *is* the exemplified systems; only that such apparatus *can be used with* the exemplified systems.

Second, none of the cited systems or patents is directed to an automated method of classifying samples. Instead, the above patents are all directed to sample preparation and automated systems of imaging prepared slides. As is clear from the specification, from claims 6-11, and the discussion above, the presently claimed methods are directed to steps taken before any sample preparation is conducted, and the claims are directed to determining whether a sample meets the criteria for being allowed to move forward to such sample preparation steps.

Further, nowhere in the art cited and discussed in the specification at page 15, lines 1-12 is there disclosed the (pre-slide preparation) acts of:

providing a cytological sample in solution in a vessel;

optically interrogating the solution with at least one wavelength of light;

determining whether a result of said interrogation meets a criterion;

attaching a positive designator to the sample vessel if the result meets the criterion; and

attaching a manipulation designator to the sample vessel if the result does not meet the criterion.

For the above reasons, Applicants respectfully request reconsideration and withdrawal of the claim rejections based on the disclosure in the Applicants' own specification.

USP 6,258,340

Claims 1-29 stand rejected under 35 U.S.C. § 102(b) for allegedly being anticipated by USP 6,258,340 ("Licha"). Applicants respectfully traverse.

Licha discloses various dyes and the use of near infrared radiation for *in vivo* diagnostic purposes. For instance, Licha states:

> This invention relates to *an in-vivo diagnostic method* based on near infrared radiation (NIR radiation) that uses water-soluble dyes and their biomolecule adducts, each having specific photophysical and pharmaco-chemical properties, as a contrast medium for fluorescence and transillumination diagnostics in the NIR range, to new dyes and pharmaceuticals containing such dyes. (Emphasis provided.) (Column 1, lines 11-19.)

> When applying the method according to the invention in in-vivo diagnosis, one or several substances of the general formula I is/are *administered to the tissues, for example, by intravenous injection*, then they are irradiated with light from the visible to the near infrared range of 650 to 1200 nm. Radiation that is not absorbed and fluorescence radiation are recorded separately or simultaneously, or against each other with a delay. A synthetic image is generated from the data obtained. (Emphasis provided.) (Column 8, lines 1-9.)

Licha teaches administering compounds to a tissue or an animal *in vivo*. Licha does not teach optically interrogating a *cytological sample in solution in a vessel*, which clearly refers to an *in vitro* process. Further, Licha does not teach attaching a positive designator or a manipulation designator to the sample vessel depending on the outcome of the comparison with a criterion. The Examiner states that the claimed attachment of positive and manipulation designators are read on the steps of recording the synthetic image and comparison to certain parameters to obtain a diagnosis. Applicants respectfully submit that this interpretation is contrary to the teachings of the specification, in view of how the claims of the application are read. As discussed above, the designators can be physically or electronically attached to the sample vessel. Licha's recording of the image does not fall within this definition of a designator. Lastly, the method of Licha is not an automated method of classifying a cytological sample; instead, it is a method of creating fluorescent images of tissue for diagnostic purposes.

Thus, Applicants respectfully submit that Licha does not teach or suggest several of the limitations of claim 1, and Applicants respectfully request reconsideration and withdrawal of the claim rejections under 35 U.S.C. § 102(b) based on Licha.

EP 0 573 535

Claims 1-29 also stand rejected under 35 U.S.C. § 102(b), for allegedly being anticipated by EP 0 573 535 ("Rava"). Applicants respectfully traverse.

Rava is directed to systems and methods of performing spectral diagnostics to diagnose the tissue in front of a fiber. See, for example, Paragraph [0018]. Rava does not teach attaching a positive designator or a manipulation designator to the sample vessel, depending on the outcome of the comparison with a criterion. The Examiner states that the claimed attachment of positive and manipulation designators may be read on the steps of recording the image and subsequent comparison to certain parameters to obtain a diagnosis. Applicants respectfully submit that this reading is contrary to the teachings of the specification. As discussed above, the

designators can be physically or electronically attached to the sample vessel. Rava's recording of the image does not fall within this definition of a designator. Lastly, the method of Rava is not an automated method of classifying a cytological sample.

Thus, Applicants respectfully submit that Rava does not teach or suggest several of the limitations of claim 1, and Applicants respectfully request reconsideration and withdrawal of the claim rejections under 35 U.S.C. § 102(b) based on Rava.

USP 5,168,066

Claims 1-29 stand further rejected under 35 U.S.C. § 102(b) for allegedly being anticipated by USP 5,168,066 ("Zahniser"). Applicants respectfully traverse.

Zahniser is directed to methods of staining and imaging cells smeared on a slide. The cells of Zahniser are not in solution in a vessel. By contrast, the presently claimed methods are directed to optically interrogating cytological samples that are in solution in a vessel. As discussed above, subsequent to the culmination of the presently claimed methods, and if the sample receives a positive designator, then a smear slide of the contents of the vessel can be prepared and the cells can then be stained and viewed. However, those steps are not claimed in the present application.

Thus, Applicants respectfully submit that Zahniser does not teach or suggest several of the limitations of claim 1, and Applicants respectfully request reconsideration and withdrawal of the claim rejections under 35 U.S.C. § 102(b) based on Zahniser.

## CONCLUSION

Based on the foregoing amendments and remarks, Applicants respectfully submit that the pending claims are now allowable over the cited references. Applicants invite the Examiner to call the undersigned if any remaining issue(s) can be resolved through a telephonic discussion.

Respectfully submitted,

Vista IP Law Group, LLP

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By: /David T. Bursc/
David T. Bursc
Registration No. 37,104